

A1
cont'd

in BVR just 2 positions downstream from the last glycine. A valine residue is invariant at the corresponding position, as in BVR, in the family of kinases that phosphorylate G-protein coupled receptors (Garcia-Bustos et al., Biochim. Biophys. ACTA 1071:83-101 (1991)). Database search results also identified additional similarities with PKGs, including a cluster of charged residues (Lys²²⁴.Arg.Asn.Arg) in the carboxy terminus of BVR. Such clusters are a characteristic of the nuclear localization signal ("NLS") (Garcia-Bustos et al., Biochim. Biophys. ACTA 1071:83-101 (1991)).

Please replace the paragraph at page 4, lines 26-30 with the following amended paragraph.

A2

Figure 1 is an image of an SDS-PAGE of hBVR subjected to immunoblotting. Phosphorylation molecular weight markers are shown on the left side (panel a) and hBVR immunoblotting on the right side (panel b). Immunoblotting used 2 µg of hBVR with a mixture (2 µg/ml each) of anti-phosphotyrosine, anti-phosphothreonine, and anti-phosphoserine ("anti-phospho mix").

Please replace the paragraph at page 6, lines 1-5 with the following amended paragraph.

A3

Figures 7A-D are images of SDS-PAGE immunoblots which illustrate that biliverdin reductase is a serine-, threonine-, tyrosine-phosphoprotein. Purified rat liver BVR (1-3 µg/ml each) was subjected to SDS-PAGE and immunoblotting with the (anti-phospho mix (2 µg/ml each) (Figure 7A), anti-phosphotyrosine (Figure 7B), anti-phosphoserine (Figure 7C), and anti-phosphothreonine (Figure 7D).

Please replace the paragraph at 6, line 30 to page 7, line 5 with the following amended paragraph.

A4

Figures 12A-C are graphs illustrating the effect of various rBVR fragments on PKC activity. Protein kinase C was incubated at 30°C with buffer or with the indicated peptides (50 µM) for 15 min prior to addition to a kinase assay using MBP as substrate. Figure 12A depicts the relative activity for each sample normalizing to that of the PKC and